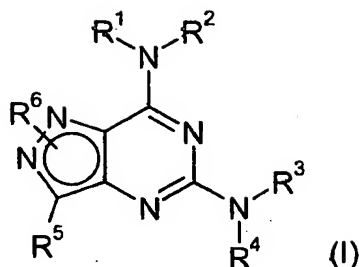


Claims

1. A compound of formula (I)



wherein

R^1 is a cyclic group selected from R^A , R^B , R^C and R^D , each of which is optionally substituted with one or more R^7 groups;

R^2 is hydrogen or C_1 - C_2 alkyl;

R^3 and R^4 are each independently C_1 - C_8 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl or C_3 - C_{10} cycloalkyl, each of which is optionally substituted with one or more R^8 groups, or R^E , which is optionally substituted with one or more R^9 groups, or hydrogen;

or $-NR^3R^4$ forms R^F , which is optionally substituted with one or more R^{10} groups;

R^5 is $-Y-CONR^{15}R^{16}$;

R^6 , which may be attached at N^1 or N^2 , is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl or C_2 - C_6 alkynyl, each of which is optionally substituted by C_1 - C_6 alkoxy, C_1 - C_6 haloalkoxy or a cyclic group selected from R^J , R^K , R^L and R^M , or R^6 is R^N , C_3 - C_7 cycloalkyl or C_3 - C_7 halocycloalkyl, each of which is optionally substituted by C_1 - C_6 alkoxy or C_1 - C_6 haloalkoxy, or R^6 is hydrogen;

R^7 is halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_{10} cycloalkyl, C_3 - C_{10} halocycloalkyl, phenyl, OR^{12} , $OC(O)R^{12}$, NO_2 , $NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}CO_2R^{14}$, $C(O)R^{12}$, CO_2R^{12} , $CONR^{12}R^{13}$ or CN ;

R^8 is halo, phenyl, C_1 - C_6 alkoxyphenyl, OR^{12} , $OC(O)R^{12}$, NO_2 , $NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}CO_2R^{14}$, $C(O)R^{12}$, CO_2R^{12} , $CONR^{12}R^{13}$, CN , R^G or R^H , the last two of which are optionally substituted with one or more R^9 groups;

R^9 is C_1 - C_6 alkyl, C_1 - C_6 haloalkyl or CO_2R^{12} ;

R^{10} is halo, C_3 - C_{10} cycloalkyl, C_3 - C_{10} halocycloalkyl, phenyl, OR^{12} , $OC(O)R^{12}$, NO_2 , $NR^{12}R^{13}$, $NR^{12}C(O)R^{13}$, $NR^{12}CO_2R^{14}$, $C(O)R^{12}$, CO_2R^{13} , $CONR^{12}R^{13}$, CN , oxo, C_1 - C_6 alkyl or C_1 - C_6 haloalkyl, the last two of which are optionally substituted by R^{11} ;

R^{11} is phenyl, $NR^{12}R^{13}$ or $NR^{12}CO_2R^{14}$;

R^{12} and R^{13} are each independently hydrogen, C_1 - C_6 alkyl or C_1 - C_6 haloalkyl;

R^{14} is C_1 - C_6 alkyl or C_1 - C_6 haloalkyl;

R^{15} and R^{16} are each independently selected from

hydrogen,

C_1 - C_6 haloalkyl,

C_1 - C_6 alkyl optionally substituted with

R^{17} ,

$-NR^{18}R^{19}$,

$-CO_2R^{20}$,

$-CONR^{21}R^{22}$,

R^{23} or

phenyl optionally substituted by

halo,

C_1 - C_6 alkyl or

R^{17} ,

C_3 - C_7 cycloalkyl optionally substituted with

C_1 - C_6 alkyl,

R^{17} or

$-NR^{18}R^{19}$, and

R^{23} ;

or $NR^{15}R^{16}$ constitutes a 3- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen, oxygen and sulphur, and which may optionally be further substituted with R^{17} , C_1 - C_6 haloalkyl, $-CO_2R^{20}$, $-CONR^{21}R^{22}$, oxo or C_1 - C_6 alkyl optionally substituted by R^{17} ;

R^{17} is hydroxy, C_1 - C_6 alkoxy, C_1 - C_6 (haloalkyl)oxy or C_3 - C_7 cycloalkyloxy;

R^{18} and R^{19} are each independently selected from hydrogen and C_1 - C_6 alkyl;

or $-NR^{18}R^{19}$ constitutes an azetidine, pyrrolidine, piperidine or morpholine ring;

R^{20} is hydrogen or C_1 - C_6 alkyl;

R^{21} and R^{22} are each independently selected from hydrogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl and C_3 - C_7 cycloalkyl;

or $-NR^{21}R^{22}$ constitutes a 3- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen, oxygen and sulphur;

R^{23} is a saturated 3- to 8-membered ring which includes at least one heteroatom selected from nitrogen, oxygen and sulphur, which ring may optionally be substituted by one or more C_1 - C_6 alkyl groups, provided that the group R^{23} is joined to the parent molecule by a covalent bond to a carbon atom of said ring;

R^A and R^J are each independently a C_3 - C_{10} cycloalkyl or C_3 - C_{10} cycloalkenyl group, each of which may be either monocyclic or, when there are an appropriate number of ring atoms, polycyclic and which may be fused to either

(a) a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

R^B and R^K are each independently a phenyl or naphthyl group, each of which may be fused to

(a) a C_5 - C_7 cycloalkyl or C_5 - C_7 cycloalkenyl ring,

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(c) a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

R^C , R^L and R^N are each independently a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated or partly unsaturated ring system containing between 3 and 10 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur, which ring may be fused to a C_5 - C_7 cycloalkyl or C_5 - C_7 cycloalkenyl group or a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

R^D and R^M are each independently a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms independently selected from nitrogen, oxygen and sulphur, which ring may further be fused to

(a) a second 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur;

(b) C_5 - C_7 cycloalkyl or C_5 - C_7 cycloalkenyl ring;

(c) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur; or

(d) a benzene ring;

R^E , R^F and R^G are each independently a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated ring system containing between 3 and 10 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

R^H is a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms independently selected from nitrogen, oxygen and sulphur; and

Y is a covalent bond, C_1 - C_6 alkylene or C_3 - C_7 cycloalkylene;

a tautomer thereof or a pharmaceutically acceptable salt, solvate or polymorph of said compound or tautomer.

2. A compound according to claim 1 wherein R^1 is R^A , which is optionally substituted with one or more R^7 groups; and

R^A is a C_3 - C_{10} cycloalkyl group, which may be either monocyclic or, when there are an appropriate number of ring atoms, polycyclic, which may be fused to either

(a) a monocyclic aromatic ring selected from a benzene ring and a 5- or 6-membered heteroaromatic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur, or

(b) a 5-, 6- or 7-membered heteroalicyclic ring containing up to three heteroatoms selected from nitrogen, oxygen and sulphur.

3. A compound according to claim 1 wherein R^1 is R^B , R^C , or R^D each optionally substituted with one or more R^7 groups, wherein

R^B is phenyl,

R^C is a monocyclic saturated or partly unsaturated ring system containing between 5 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur,

R^D is furanyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, isothiazolyl, thiazolyl, oxadiazolyl, pyridyl, pyridazinyl, pyrimidyl or pyrazinyl, and

R^7 is fluoro, methyl, ethyl, hydroxy, methoxy, propoxy or CONHMe.

4. A compound according to any one of claims 1 to 3 wherein R^2 is hydrogen or methyl.

5. A compound according to any one of claims 1 to 4 wherein R^3 is hydrogen or C_1 - C_4 alkyl, which is optionally substituted with one or more R^8 groups, or R^3 is azetidiny, pyrrolidinyl or piperidinyl, each of which is optionally substituted with one or more R^8 groups, wherein

R^8 is hydroxy, methoxy, methoxyphenyl, NH_2 , NHMe, NMe_2 , $NHCO_2^tBu$, $NMeCO_2^tBu$, CO_2H , CONHMe, pyrrolidinyl, piperidinyl, morpholinyl or pyrazolyl, the last four of which are optionally substituted with one or more R^9 groups, and

R^9 is methyl or CO_2^tBu .

6. A compound according to any one of claims 1 to 5 wherein R^4 is hydrogen, methyl or ethyl.

7. A compound according to any one of claims 1 to 6 wherein $-NR^3R^4$ forms R^F , which is optionally substituted with one or more R^{10} groups, wherein

R^F is selected from azetidiny, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, 3-azabicyclo[3.1.0]hex-3-yl, homopiperazinyl, 2,5-diazabicyclo[4.3.0]non-2-yl, 3,8-diazabicyclo[3.2.1]oct-3-yl, 3,8-diazabicyclo[3.2.1]oct-8-yl, 1,4-diazabicyclo[4.3.0]non-4-yl and 1,4-diazabicyclo[3.2.2]non-4-yl, and

R^{10} is halo, methyl, ethyl, isopropyl, hydroxy, methoxy, NH_2 , NHMe, NMe_2 , $NHCO_2^tBu$, CO_2H , CO_2^tBu , oxo, benzyl, $-CH_2NH_2$, $-CH_2NHMe$, CH_2NMe_2 or $-CH_2NMeCO_2^tBu$.

8. A compound according to any one of claims 1 to 7 wherein

R^{15} and R^{16} are each independently selected from hydrogen, C_1 - C_6 alkyl optionally substituted with R^{17} , $-NR^{18}R^{19}$, $-CO_2R^{20}$, $-CONR^{21}R^{22}$, R^{23} or phenyl optionally substituted by halo, C_1 - C_6 alkyl or R^{17} , C_3 - C_7 cycloalkyl and R^{23} , or $NR^{15}R^{16}$ constitutes a 5- to 7-membered ring which may optionally include one or more further heteroatoms selected from nitrogen and oxygen, and which may optionally be further substituted with R^{17} , $-CO_2R^{20}$, $-CONR^{21}R^{22}$ or C_1 - C_6 alkyl optionally substituted by R^{17} ;

R^{17} is hydroxy, C_1 - C_6 alkoxy or C_3 - C_7 cycloalkyloxy;

R^{21} and R^{22} are each independently selected from hydrogen, C_1 - C_6 alkyl, and C_3 - C_7 cycloalkyl, or $-NR^{21}R^{22}$ constitutes a 5- to 8-membered ring which may optionally include one or more further heteroatoms selected from nitrogen and oxygen; and

R^{23} is a saturated 5- to 7-membered ring which includes at least one heteroatom selected from nitrogen and oxygen, which ring may optionally be substituted by one or more C_1 - C_6 alkyl groups.

9. A compound according to any one of claims 1 to 8 wherein R^6 is positioned on N^1 .
10. A compound according to claim 9 wherein R^6 is hydrogen, methyl, ethyl, isopropyl, isobutyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, 2,2,2-trifluoroethyl, tetrahydrofuranylmethyl, tetrahydropyranylmethyl, tetrahydropyranyl or pyridinylmethyl.
11. A compound according to claim 1 wherein

R^1 is a cyclic group selected from R^A , R^B , R^C and R^D , each of which is optionally substituted with one or more R^7 groups;

R^7 is halo, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, OR^{12} or $CONR^{12}R^{13}$;

R^8 is halo, phenyl, C_1 - C_6 alkoxyphenyl, OR^{12} , $NR^{12}R^{13}$, $NR^{12}CO_2R^{14}$, CO_2R^{12} , $CONR^{12}R^{13}$, R^G or R^H , the last two of which are optionally substituted with one or more R^9 groups;

R^A is a monocyclic C_5 - C_7 cycloalkyl group;

R^B is phenyl;

R^C is a monocyclic saturated ring system containing between 5 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

R^D is a 5-membered heteroaromatic ring containing a heteroatom selected from nitrogen, oxygen and sulphur and optionally up to two further nitrogen atoms in the ring, or a 6-membered heteroaromatic ring including 1, 2 or 3 nitrogen atoms;

R^E is a monocyclic saturated ring system containing between 3 and 7 ring atoms containing one nitrogen atom;

R^F is a monocyclic or, when there are an appropriate number of ring atoms, polycyclic saturated ring system containing between 3 and 10 ring atoms containing at least one nitrogen atom and optionally one other atom selected from oxygen and sulphur;

R^6 is a monocyclic saturated ring system containing between 3 and 7 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur; and

R^H is a 5- or 6-membered heteroaromatic ring containing up to two nitrogen atoms.

R^3 is hydrogen, C_1 - C_4 alkyl, which is optionally substituted with one or more R^8 groups, or R^E , which is optionally substituted with one or more R^9 groups;

R^4 is hydrogen, C_1 - C_6 alkyl or C_1 - C_6 haloalkyl;

or $-NR^3R^4$ forms R^F , which is optionally substituted with one or more R^{10} groups;

R^6 is C_1 - C_4 alkyl or C_1 - C_4 haloalkyl, each of which is optionally substituted by C_1 - C_4 alkoxy, C_1 - C_4 haloalkoxy or a cyclic group selected from R^J , R^L and R^M , or R^6 is R^N or hydrogen;

R^J is cyclopropyl or cyclobutyl;

R^L and R^N are each independently a monocyclic saturated ring system containing either 5 or 6 ring atoms, of which at least one is a heteroatom selected from nitrogen, oxygen and sulphur;

R^M is a 5- or 6-membered heteroaromatic ring containing a heteroatom selected from nitrogen, oxygen and sulphur; and

Y is a covalent bond.

12. A compound according to claim 1 selected from:

1-(2-ethoxyethyl)-*N*-ethyl-5-(ethylamino)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-(methylamino)ethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-*N*-(2-(dimethylamino)ethyl)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-*N*-(piperidin-4-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-methoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

(2*R*)-2-[[5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carbonyl]amino}propionic acid,

3-[[5-(dimethylamino)-1-(2-ethoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carbonyl]amino}propionic acid,

1-(2-ethoxyethyl)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-5-(piperazin-1-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-methyl-5-((3*R*)-3-methylpiperazin-1-yl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-ethyl-5-((3*R*)-3-methylpiperazin-1-yl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(ethylamino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-*N*-(2-methoxyethyl)-5-(methylamino)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

5-(dimethylamino)-1-(2-ethoxyethyl)-*N*-(2-hydroxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(ethylamino)-*N*-(2-methoxyethyl)-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-(*N*-(2-hydroxyethyl)-*N*-methylamino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

1-(2-ethoxyethyl)-5-((2-methoxyethyl)amino)-*N*-methyl-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide,

7-(cyclohexylamino)-1-(2-ethoxyethyl)-*N*-methyl-5-((3*R*)-3-methylpiperazin-1-yl)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide, and

1-(2-ethoxyethyl)-*N*-methyl-5-[*N*-methyl-*N*-((3*S*)-1-methylpyrrolidin-3-yl)amino]-7-(4-methylpyridin-2-ylamino)-1*H*-pyrazolo[4,3-*d*]pyrimidine-3-carboxamide

and tautomers thereof and pharmaceutically acceptable salts, solvates and polymorphs of said compound or tautomer.

13. A pharmaceutical composition comprising a compound of formula (I) as claimed in any one of claims 1 to 12, or pharmaceutically acceptable salts, solvates or polymorphs thereof, and a pharmaceutically acceptable diluent or carrier.

14. A compound of formula (I) as claimed in any one of claims 1 to 12, or a pharmaceutically acceptable salt, solvate or polymorph thereof, for use as a medicament for the treatment of a disease or condition selected from hypertension (including essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension), congestive heart failure, angina (including stable, unstable and variant (Prinzmetal) angina), stroke, coronary artery disease, congestive heart failure, conditions of reduced blood vessel patency (such as post-percutaneous coronary angioplasty), peripheral vascular disease, atherosclerosis, nitrate-induced tolerance, nitrate tolerance, diabetes, impaired glucose tolerance, metabolic syndrome, obesity, sexual dysfunction (including male erectile disorder, impotence, female sexual arousal disorder, clitoral dysfunction, female hypoactive sexual desire disorder, female sexual pain disorder, female sexual orgasmic dysfunction and sexual dysfunction due to spinal cord injury), premature labour, pre-eclampsia, dysmenorrhea, polycystic ovary syndrome, benign prostatic hyperplasia, bladder outlet obstruction, incontinence, chronic obstructive pulmonary disease, acute respiratory failure, bronchitis, chronic asthma, allergic asthma, allergic rhinitis, gut motility disorders (including irritable bowel syndrome), Kawasaki's syndrome, multiple sclerosis, Alzheimer's disease, psoriasis, skin necrosis, scarring, fibrosis, pain (particularly neuropathic pain), cancer, metastasis, baldness, nutcracker oesophagus, anal fissure and haemorrhoids.

15. Use according to claim 14 wherein the disease or condition is selected from essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension.